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10/527,950	09/30/2005	Timothy P. Tully	17VV-137226	1059

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EXAMINER

DUTT, ADITI

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/527,950	<b>Applicant(s)</b> TULLY ET AL.	
	<b>Examiner</b> Aditi Dutt	<b>Art Unit</b> 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-10,12-15,17-22,24 and 25 is/are pending in the application.
- 4a) Of the above claim(s) 17,18 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,6-10,12-15,19-22 and 24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/17/08</u> .   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of Claims***

1. The amendments filed on 17 July 2008 have been entered into the record and have been fully considered. Claims 5, 11, 16 and 23 have been cancelled. Claims 1, 7, 8, 12, 13 and 19 are amended.
2. Claims 1-4, 6-10, 12-15, 19, 20-22 and 24, drawn to a method of identifying candidate compounds for enhancing CREB pathway function and assessing the effect on CREB-dependent gene expression, are under consideration in the instant application.
3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants response and withdrawn.
4. Applicant's arguments filed on 17 July 2008, have been fully considered. New grounds of objection and rejection are as follow.

### ***Response to Amendment***

#### **Withdrawn objections and/or rejections**

5. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (17 July 2008).
6. The rejection of claims 1-4, 5-10, 19-22 and 24 under 35 U.S.C. 112, first paragraph (scope of enablement) is withdrawn, in view of the claim amendments.

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7. The rejection of 1, 2, 7, 8, 13 and 19, under 35 U.S.C. 112, second paragraph is withdrawn, because of the amendment of relevant claims and Applicant's persuasive argument.

Rejections Maintained

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The rejection of claims 1, 3-7, 9-12, 14, and 16 under 35 U.S.C. 103(a) as being unpatentable over Sheriff et al., (Reg Pept 75-76: 309-318, 1998), in view of Herzog et al. (PNAS 89: 5794-5798, 1992), is applied to amended claims 1, 3-4, 6-7, 9, 12 and 14-15, for reasons of record in the Office Action dated 17 April 2008. It is noted that page 11, para 21, line 1 of the previous Office Action dated 17 April 2008 had a typographical error, wherein claim 15 was inadvertently missing, although the claim was considered and rejected in that rejection.

Examiner apologises for the lapse

9. Applicant argues that Sheriff does not teach that control cells treated with NPY and not with forskolin do not exhibit significantly different activity from control cells not treated with forskolin or NPY. Quoting Sheriff, Applicant alleges

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that Examiner's interpretation is contrary to Sheriff's teaching, "i.e. those of ordinary skill in the art", because Sheriff teaches that forskolin and NPY increase luciferase activity, and that this "may involve more than one member of CRE binding transcription factors". Applicant further asserts that Sheriff's teaching was directed to "elucidating downstream signal transduction pathways beyond the second messenger levels involved in NPY-mediated actions", and Herzog's teaching was drawn to "elucidating receptor subtypes that mediate observed effects of NPY". Furthermore, based on the current claim amendments, Applicant cautions that since Sheriff and the other references do not teach or suggest the screening a plurality of compounds for potential development of candidate cognitive enhancer compounds in the claimed screening method, "any attempt to read these limitations into the cited art would constitute nothing more than hindsight reconstruction on the part of the Examiner".

10. Applicant's arguments are fully considered, however, are not found to be persuasive. Firstly, it is reinstated that Sheriff et al. demonstrate that the luciferase activity in control cells treated with NPY but not with forskolin is not significantly different from the activity elicited by control cells that are not treated with either forskolin or with NPY (Figure 5, 1<sup>st</sup> and 2<sup>nd</sup> bar), thereby denying Applicant's allegation that this effect is not observed. Additionally, the treatment of the transfected cells with NPY and forskolin results in a significant increase of luciferase activity as compared to control cells treated with forskolin but not with the NPY (Abstract; Results: Section 3.5; Figure 5, 5<sup>th</sup> and 6<sup>th</sup> bar). Applicant's

allegation that Sheriff's teaching is contrary to Examiner's interpretation is mistaken, because of the observations matching the requirements in the claimed method as stated above. The claim recites the effect of a compound on CREB pathway in the presence of a CREB stimulating agent forskolin. Comparable results from an identical experimental design is presented in Figure 5 of the Sheriff paper, whereby it is evident that no contradiction exists with the author or the person of ordinary skill as alleged by Applicant. Furthermore, Applicant's argument over the mechanism of action, receptor subtypes and signal transduction pathways involved in NPY and CREB interaction taught in the cited references is beyond the scope of the claimed limitations. The claim plainly requires the effect of a test substance on enhancing CREB pathway function in the presence of forskolin, which is indicated by activity of the indicator gene or by gene expression studies. The claims do not require that the test substance is not involving more than one member of CRE binding transcription factors.

Furthermore, Applicant repeatedly alleges reminding Examiner of the missing "plurality of test compounds" from the cited references. Applicant also presents a cautionary note stating not to attempt reading this limitation into the references, or else will amount to "hindsight reasoning". However, it is taught in the Sheriff paper that NPY exerts several biological and cognitive functions (e.g. modulation of memory, inhibition of anxiogenic activity, feeding behavior, etc.), by activating the CREB pathway. Additionally, as evidenced by Impey et al., "CREB is a key regulator of long-term memory consolidation" (Nature Neurosc 1: 595-601, 1998;

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page 595, para 2). It would, therefore, be obvious to the person of ordinary to test a plurality of cognitive enhancer compounds like NPY that would stimulate the CREB pathway, using the same method steps as taught in the Sheriff and Herzog references. The person of ordinary skill would be motivated to test multiple compounds because both, the CREB pathway and NPY have known cognitive modulatory effects. Applicants may argue that the examiner's conclusion of obviousness is based on improper hindsight reasoning. However, "[a]ny judgement on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper." *In re McLaughlin* 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971). Applicants may also argue that the combination of two or more references is "hindsight" because "express" motivation to combine the references is lacking. However, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See *Ruiz v. A.B. Chance Co.*, 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). \*\*>See MPEP § 2141 and § 2143 for guidance regarding establishment of a *prima facie* case of obviousness. Lastly, "screening a plurality of compounds" is part of the preamble of the claim reciting the screening method, that reflects a general feature of any screening protocol without providing further limitations to the invention.

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Additionally, screening implies testing more than one compound. Therefore, the addition of the limitation "plurality of compounds" does not add any distinct limitation to the claimed method, rather is redundant. If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also *Rowe v. Dror*, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997). Because of the above reasons, the claimed invention stays rejected as *prima facie* obvious over the combined teachings of the prior art.

11. The rejection of claims 19(a-k), and 20-24 under 35 U.S.C. 103(a) as being unpatentable over Sheriff et al., (Reg Pept 75-76: 309-318, 1998), in view of Herzog et al. (PNAS 89: 5794-5798, 1992), and further in view of Barad et al. (PNAS 95: 15020-15025, 1998), is applied to amended claims 19, 20-22 and 24, for reasons of record in the Office Action dated 17 April 2008.
12. Applicant repeats the same argument as above, stating that neither Sheriff nor Herzog teaches or suggests screening a plurality of compounds to determine the ability of compounds to enhance the CREB pathway and identify the compounds as a candidate cognitive enhancer compound based on the claimed



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invention, nor does Barad remedy the deficiencies. Applicants thus request the withdrawal of the rejection.

13. Applicant's arguments are fully considered, but not found to be persuasive based on the detailed discussion presented above. As stated in the previous Office Action it is reiterated that it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method for elevating Y1 message in neuroblastoma cells as taught by Sheriff et al., by using *hippocampal neurons*. It would have also been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method for elevating Y1 message in neuroblastoma cells as taught by Sheriff et al., by elevating cAMP levels from hippocampal slices as taught by Barad et al. The person of ordinary skill in the art would have been motivated to substitute hippocampal neurons for hippocampal slices, because neurons are individual cells that would elicit the CREB dependent gene expression in a cell specific manner. Thus, the claimed invention as a whole stays rejected as *prima facie* obvious over the combined teachings of the prior art.

14. The rejection of claims 2, 8 and 13 under 35 U.S.C. 103(a) as being unpatentable over Sheriff et al., (Reg Pept 75-76: 309-318, 1998), in view of Herzog et al. (PNAS 89: 5794-5798, 1992), and further in view of Barad et al. (PNAS 95: 15020-15025, 1998), is applied to amended claims, for reasons of record in the Office Action dated 17 April 2008.

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15. Applicant repeats the same argument as above, with emphasis directed to the screening of a plurality of compounds to identify the compounds as a candidate cognitive enhancer compound based on the claimed invention. Applicants thus request the withdrawal of the rejection.
16. Applicant's arguments are fully considered, but not found to be persuasive based on the detailed discussion presented above. As stated in the previous Office Action it is reiterated that it would have been obvious to the person of ordinary skill in the art at the time the claimed invention was made to determine the sequential addition of compounds to be added to neuroblastoma cells or hippocamal cells for identifying compounds that enhance the CREB pathway function, as taught by Sheriff et al., or Barad et al. The person of ordinary skill in the art would have been motivated to perform such tests, to assess the optimum conditions to achieve the desirable increase in CREB function. The person of ordinary skill in the art would have expected success because in vitro cell based assays using one or more agents were routinely performed in the scientific and medical community, at the time the invention was made. Thus, the claimed invention as a whole stays rejected as *prima facie* obvious over the combined teachings of the prior art.

***Conclusion***

17. No claims are allowed.
18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
19. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.
20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.
21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The

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fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD  
24 October 2008

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649